



**UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office**

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/398,610	09/17/99	EDGE	M 10275/137001

LOUIS MYERS
FISH & RICHARDSON PC
225 FRANKLIN STREET
BOSTON MA 02110-2804

HM22/0913

EXAMINER

BECKER, EG, A

ART UNIT

PAPER NUMBER

1632

DATE MAILED:

09/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.		Applicant(s)	
	09/398,610		EDGE ET AL.	
	Examiner		Art Unit	
	Anne M Beckerleg		1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 June 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) 9-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 September 1999 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>7</u> . | 6) <input type="checkbox"/> Other: |

Art Unit: 1632

DETAILED ACTION

Applicant's response to the restriction/election requirement received on 6/22/01 has been entered. Applicant's election without traverse of the species, fusion proteins comprising angiogenin, is acknowledged. Claims 1-17 are pending in the instant application. Please note, the claims submitted with the application listed two claims 15. The second claim 15 and claim 16 have been renumbered according to Rule 126 as claims 16 and 17. Based on applicant's election, claim 9 is withdrawn as being drawn to subject matter non-elected without traverse in paper no. 8. Claims 1-8, and 10-17 are elected for prosecution in the instant application. An action on the merits follows.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 16-17 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The applicant claims a transgenic animal. As humans are considered animals, this claims reads on a transgenic human. Human beings are not considered

Art Unit: 1632

patentable subject matter. This rejection can be overcome by amending the claims to recite a "non-human transgenic animal".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "e.g." renders the claims indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 15 is rejected as failing to define the invention in the manner required by 35 U.S.C. 112, second paragraph. The claim is narrative in form following step (f) and replete with indefinite and functional or operational language. The claim must be in one sentence form only. It appears as the claim should end with step (f). However, following this step, the claim recites two additional narrative sentences that appear to describe pharmaceutical compositions of a fusion protein and milk that are completely separate and patentably distinct inventions from the isolated nucleic acid construct claimed in the preamble of claim 15. If the applicant intends to additionally claim compositions of fusion proteins, it is necessary to provide a separate claim(s) which recites this limitations of this invention. However, it is noted that based on the elected subject matter, i.e.

Art Unit: 1632

transgenic animals and isolated nucleic acids, the addition of claims drawn to protein compositions would result in restriction of those claims from the subject matter of claims 1-17. It is suggested that the applicant amend claim 15 to delete the lines following the conclusion of step (f) in order to overcome this grounds of rejection.

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 16 recites, "... a fusion protein described in claim." However, no claim is actually recited. Therefore, it is confusing as to what are the characteristics of the fusion protein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

Art Unit: 1632

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8, and 10-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,959,171, 9/28/99, filed on 8/17/94, hereafter referred to as Hyttinen et al., in view of Zewe et al. (1997) Immunotech., Vol. 3 (2), 127-136. The applicant claims a vector encoding a mammary epithelial specific promoter, a signal sequence that directs the secretion of a fusion protein, and a fusion protein that comprises angiogenin, a transgenic animal which comprises said vector, and methods of making a fusion protein providing a transgenic animal which expresses a fusion protein comprising angiogenin, and recovering the fusion protein from the milk of the transgenic animal. The applicant also claims said methods wherein the fusion protein comprising angiogenin further comprises a subunit of an Ig specific for a tumor antigen selected from a group which includes transferrin receptor. The applicant further claims said transgenic animals and methods wherein the fusion protein is secreted into the milk of the transgenic animal at concentrations of at least about 1 mg/ml.

Hyttinen et al. teaches vectors encoding a fusion protein operatively linked to regulatory elements needed for high level mammary gland specific expression derived from a milk protein gene or a mammary tumor virus and a DNA sequence encoding a signal sequence needed for secretion and maturation of the fusion protein (Hyttinen et al., column 3). Hyttinen et al. also teaches transgenic animals made using said vectors, and methods of making a fusion protein comprising collecting milk from a transgenic mammal which expresses a fusion protein in its milk,

Art Unit: 1632

and isolating the recombinant fusion protein from the milk (Hyttinen et al., column 3). Hyttinen et al. further teaches that making and using a transgenic mouse which expresses a beta-lactoglobulin-hEPO fusion protein at concentrations of 0.2-1 mg/ml in the transgenic milk (Hyttinen et al., column 10, lines 30-35). Hyttinen also teaches that the general idea of making and using transgenic bioreactors for the production of large quantities of proteins, particularly human proteins, was suggested as early as 1986 and that numerous examples of transgenic bioreactors exist in the art, citing references from 1991-1992 (Hyttinen et al., column 1). Thus, Hyttinen establishes that the art recognized the advantages of producing large quantities of biologically relevant, therapeutic proteins in milk of transgenic animals.

Although Hyttinen et al. teaches general methods for making transgenic animals comprising fusion proteins and methods of making and isolating fusion proteins from the milk of transgenic mammals, Hyttinen et al. differs from the instant invention by not specifically teaching the production of a fusion protein comprising angiogenin. Zewe et al. supplements Hyttinen et al. by teaching nucleic acid expression constructs which encode a fusion protein comprising a single chain antibody against the transferrin receptor and angiogenin (Zewe et al., abstract). Zewe et al. also teaches that the isolated fusion proteins are capable of inhibiting protein synthesis in human tumor cell lines (Zewe et al., abstract). While Zewe et al. teaches the expression of the fusion protein in bacteria, the skilled artisan would have been motivated to express the fusion protein taught by Zewe et al. using a mammalian bioreactor system in order to produce larger quantities of the human fusion protein as taught by Hyttinen et al., and in order to avoid the contamination

Art Unit: 1632

of the fusion proteins with bacterial toxins. The undesirability of using recombinant proteins derived from bacteria in humans was extremely well known at the time of filing. Therefore, in view of the benefits of using a transgenic bioreactor to produce large quantities of a protein for use in humans, it would have been *prima facie* obvious to the skilled artisan to express the fusion protein taught by Zewe et al. using the transgenic bioreactors taught by Hyttinen. Further, based on successful use of transgenic bioreactors in expressing large quantities of a variety of human proteins and fusion proteins as taught by Hyttinen et al., the skilled artisan would have had a reasonable expectation of success in expressing the fusion protein comprising the a single chain antibody against the transferrin receptor and angiogenin in the milk of a transgenic mammal according to the methods taught by Hyttinen et al.

Claim Objections

Claim 5 is objected to because of the following informalities: transferrin receptor is misspelled as “transferring receptor”. Appropriate correction is required.

Claim 17 is objected to because of the following informalities: the term 0.5 mg/ml is misspelled as “0.5 mg/ml”. Appropriate correction is required.

No claims are allowed.

Art Unit: 1632

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Beckerleg, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Thurs and every other Friday from 8:30-6:00. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The art unit fax number is (703) 308-8724.

Dr. A.M.S. Beckerleg

**A.M.S. BECKERLEG
PATENT EXAMINER**

A handwritten signature in black ink, appearing to read 'A.M.S. BECKERLEG', followed by a horizontal line.

Attachment for PTO-948 (Rev. 03/01, or earlier)

6/18/01

The below text replaces the pre-printed text under the heading, "Information on How to Effect Drawing Changes," on the back of the PTO-948 (Rev. 03/01, or earlier) form.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the Notice of Allowability. Extensions of time may **NOT** be obtained under the provisions of 37 CFR 1.136(a) or (b) for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a).

Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.